## REMARKS

Status of the Claims

Claims 1, 4-7 and 10-12 are pending. Claims 1, 4-7 and 10-12 are rejected. Claims 1 and 7 are amended.

Claim amendments

Claims 1 and 7 are amended to overcome the claim objections and 35 U.S.C 112, second paragraph rejection. Amended claim 1 is directed to a transductionally and transcriptionally modified adenoviral vector with improved efficacy at the target site and reduced transgene expression at the non-target site *in vivo* compared to an adenoviral vector without the transductional and the transcriptional modification. This modified adenoviral vector comprises: (i) a targeting component that targets the vector to specific target cell, wherein the targeting component comprises a bi-specific antibody conjugate linking a Fab fragment of an anti-Ad5 knob antibody with an anti-angiotensin converting enzyme antibody wherein an angiotensin converting enzyme molecule is expressed on the target cells; and (ii) a tissue specific promoter that drives the expression of a transgene carried by the vector in the target cells.

Amended claim 7 is directed to a method of increasing targeting specificity to target cells and reducing transgene expression in non-target cells by an adenoviral vector. This method comprises the step of: contacting target cells with an adenoviral vector comprising the same components as described in

amended claim 1, wherein the adenoviral vector has increased targeting specificity to the target cells and results in reduced transgene expression in non-target cells as compared to adenoviral vector without the targeting component and the tissue specific promoter.

Inventorship

The Examiner states that the inventorship of this non-provisional application under 37 CFR 1.48(a) is deficient because it does not include a statement from Danilov, Sergei M. (an inventor that was added) stating that the error occurred without deception.

Applicants submit a statement from Dr. Sergei M. Danilov, stating that the error occurred without deception along with the response to this Office Action.

Oath/Declaration

The Examiner states that the declaration is defective since non-initialed and/or non-dated alterations have been made to the oath or declaration.

Applicants submit an amended oath/declaration along with the response to this Office Action.

Specification

The Examiner states that the disclosure needs correction since in the "Brief Description of the Drawings" section (pages 10-12), Figures 2, 3, 4, 5,

6 and 7 are referred despite the existence of Figures 2A-C, 3A-D, 4A-C, 5A-B, 6A-F and 7A-C.

Applicants have amended the figure legends in the "Brief Description of the drawings" to correspond to indicated figures.

Claim Objections

The Examiner objects to claim 1 because it ends with a comma instead of a period and to claim 7 because it lacks an article "an" in front of the term "adenoviral vector" in line 3 of the claim.

Applicants have replaced the comma with a period (claim 1) and incorporated "an" in front of the term "adenoviral vector" (claim 7). Accordingly based on these amendments, Applicants request the withdrawal of claim objections.

The 35 U.S.C. §112, First Paragraph Rejection

Claims 4-6 and 10-12 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement because the claims contain subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The Examiner states that although the anti-angiotensin converting enzyme monoclonal antibody 9B9 described in the instant invention is readily

available to the public, it is unclear whether anti-Ad5 knob antibody 1D6.14 is also readily available to the public or that written instructions are sufficient to reproducibly construct the bi-specific antibody conjugate linking 1D6.14 antibody with 9B9 antibody from starting materials known and readily available to the public. Accordingly, availability of such biological material is deemed necessary to satisfy the enablement provisions of 35 U.S.C. 112.

The Examiner has required Applicant to make a deposit. Applicants assure that the deposit will be timely made and will provide evidence of said deposit promptly.

The 35 U.S.C. §112, Second Paragraph Rejection

Claims 1, 4-7 and 10-12 stand rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as invention. Applicants respectfully traverse this rejection.

The Examiner states that it is unclear as to what is encompassed by the phrase "with improved efficacy at the target site and reduced transgene expression at the non-target site" in claim 1 and its dependent claims.

As discussed earlier, Applicants have amended claim 1 which now recites a transductionally and transcriptionally modified adenoviral vector with improved efficacy at the target site and reduced transgene expression at the non-target site *in vivo* compared to an adenoviral vector without the transductional and the transcriptional modification.

With regards to claims 1 and 7, the Examiner states that the limitation "said angiotensin converting enzyme molecule" in lines 9-10 of the claim 1 and in lines 8-9 of claim 7 has insufficient antecedent basis in the claim and needs clarification.

As discussed earlier, the term "said" in front of "angiotensin converting enzyme molecule" is replaced with "an" in amended claims 1 and 7. Accordingly based on these amendments, Applicants respectfully request the withdrawal of rejections of claims 1, 4-7 and 10-12 under 35 U.S.C 112, second paragraph.

This is intended to be a complete response to the Office Action mailed July 28, 2004. Applicants submit that the pending claims are in condition for allowance. If any issues remain outstanding, please telephone the undersigned attorney of record for immediate resolution.

Respectfully submitted,

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